Staphylococcus Aureus: Golden Grapes

- Gram positive coccus in clusters
- Catalase positive
- Beta hemolytic
- Facultatively anaerobic
Protein Arsenal

- **Protein A**: Protects against opsonization and phagocytosis by binding Fc portion of IgG
- **Coagulase**: Protects from phagocytosis by fibrin formation
- **Hemolysins-alpha, beta, gamma, delta**: Destroys RBCs, neutrophils, platelets, macrophages
- **Leukocidins**: Destroys leukocytes
- **Penicillinase**: Secreted form of beta-lactamase that inactivates antibiotics by disrupting the beta-lactam portion of PCN
- **Novel PCN Binding Protein**: Transpeptidase necessary for cell wall peptidoglycan formation. Inhibited by PCN
- **Hyaluronidase, staphylokinase, lipase, protease**: Lyse proteoglycans, fibrin clots, fats, and proteins to facilitate bacterial spread
Exotoxin Arsenal

- Toxic Shock Syndrome Toxin (TSST-1)
  - Pyrogenic toxins binds to MHC class II molecules on antigen presenting cells.
  - Leads to non-specific, polyclonal T-cell activation with resulting massive cytokine release
- Exfoliative Toxins (Scalded Skin Syndrome)-Sloughing of skin
- Enterotoxin Heat Stable Toxins (Food Poisoning)-Vomiting, diarrhea
Pssst! Hey kid! Wanna be a Superbug...? Stick some of this into your genome... Even penicillin won't be able to harm you...!

It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.
History 101
- 1928 Alexander Fleming discovered PCN, the super drug! Used for any type of minor infection.
- 1943 PCN used for *S. aureus* infections
- 1947 First strains of PCN resistant *S. aureus*
- 1950s resistance rendered PCN ineffective for *S. aureus*
- 1959 Methicillin developed by Beecham
- 1961 UK hospital reported first strain of MRSA
- 1968 First US case of MRSA in a Boston man. However, MRSA remained isolated to those immunocompromised and recently hospitalized
- 1970's First major MRSA outbreak in Eastern Australia. MRSA spread throughout Europe, with many health cares centers affected
- 1980s resistance in the US spread from mainly IVDU and immunocompromised to healthcare workers, prisoners
Methicillin-Resistant Staphylococcus Aureus

- MRSA-Strain of *S. aureus* with acquired multiple drug resistance
- Resistance-Conferred through mobile genetic elements such as bacteriophages, plasmids, and pathogenicity islands which transform commensal organisms into pathogenic organisms
- *Staphylococcal* Cassette Chromosome Mec (*SCCmec*)- mobile genetic element coding for the chromosomal segment *MecA*
- *MecA*-encodes for an altered PCN binding protein 2A (PBP2a)
- PBP2a: Altered component of the cell wall that lowers the affinity for binding *β*-lactams (PCN, oxacillin, cephalosporins, carbapenems)
- Penicillinase: Cleaves *β*-Lactam ring of PCN
B-lactamase enzyme cleaves C-N bonds

Foster, TJ. The Staphylococcus aureus "superbug" J Clin Invest. 2004; 114(12):1693
The Problem

- 20% of the population are persistently colonized by *S. aureus*. 30% acquire it intermittently \(^1,4\)
- 1.5% of the US population are colonized with MRSA \(^1\)
- MRSA accounts for 40-60% of the *S. aureus* isolates in some healthcare institutions \(^3\)
- The prevalence of MRSA colonization in US adult ICUs is approximately 8% (ranges 5-20%) \(^4\)
- The risk of MRSA infection among MRSA-colonized patients varies from 10% to 25% \(^4\)
- Compared to MSSA, MRSA infections carry a 40% higher mortality \(^4\)
A Very Expensive Problem

• Compared to MSSA, an infection with MRSA increase cost $3,000-$35,000 ³

• Excluding indirect costs, MRSA infections cost the healthcare system an extra $830 million to $9.7 billion ³

MRSA Statistical References


Dec; 13(12). www.cdc.gov/eid

A Growing Problem

• Increasing prevalence: 2% of USA ICU S. aureus infections were MRSA in 1974, 22% in 1995, 64% in 2004

• In 2005...

• 278,000 MRSA related hospitalizations

• 94,360 people developed invasive MRSA infections

• 85% of invasive MRSA infections were healthcare associated

• 18,650 MRSA related deaths during hospitalization

• Approximately equal to deaths from AIDS, TB, and hepatitis combined
"The patient in the next bed is highly infectious. Thank God for these curtains."
Surfaces commonly contaminated by MRSA
(Methicillin-resistant *staphylococcus aureus*)

R. S. Ulrich with P. A. Wilson
Strategies Overseas: Search and Destroy

• Netherlands: <1% prevalence of MRSA
• Finland: 0.5% prevalence of MRSA
• Denmark: <1% prevalence of MRSA
• Sweden and Norway <2% prevalence of MRSA
• Belgium 28%, France 33%, Germany 19%


MRSA Prevalence Is High Globally

- UK (44%)
- Germany (19%)
- Spain (23%)
- Italy (38%)
- France (33%)
- Netherlands (<1%)
- China (39%)
- Japan (74%)
- Taiwan (61%)
- Hong Kong (80%)
- Singapore (63%)
- Australia (30%)
- Latin America (29%)
- South Africa (49%)
- Nigeria (21%)

The Policy

- Screening of high-risk patients (those with a previous h/o MRSA, from a hospital with a high MRSA prevalence, hospitals in other countries, job working with pigs and calves)
- Screening of other patients and personal in contact with MRSA carriers
- Isolation of MRSA positive patients and staff
- Disinfection of skin, hair, and nasal passages of MRSA carriers (personnel must screen negative before working with MRSA free patients)
- “Outbreak” (2 or more MRSA infections) disaster plan
Catching on...

- In mid 2000 numerous European countries with endemic MRSA initiated or intensified infection control measures including
  - Screening for MRSA, isolation, decontamination
  - Hand hygiene
  - Antibiotic stewardship
Figure 1. Trends of decreases in the percentage of S. aureus bacteremia cases caused by methicillin-resistant S. aureus (MRSA) in 10 countries reporting to the European Antibiotic Resistance Surveillance System, 2005–2008. Adapted with permission from the European Antimicrobial Resistance Surveillance System 2008 annual report.1

May 2003, the Society for Healthcare Epidemiology of America (SHEA) published guidelines for preventing nosocomial transmission of MRSA and vancomycin-resistant enterococci.

CONCLUSION:

“Active surveillance cultures are essential to identify the reservoir for spread of MRSA and VRE infections and make control possible using the CDC’s long-recommended contact precautions.”

Infect Control Hosp Epidemiol 2003;24:362-386
Controversies

• Efficacy?
• Cost?
• Patient satisfaction?
Contact Precautions: Not Just for Style Points

Detection of Methicillin-Resistant *Staphylococcus aureus* and Vancomycin-Resistant Enterococci on the Gowns and Gloves of Healthcare Workers

Snyder, Graham M. MD; Thom, Kerri A. MD; Furuno, Jon P. PhD; Perencevich, Eli N. MD, MS; Roghmann, Mary-Claire MD, MS; Strauss, Sandra M. BS MT(ASCP); Netzer, Giora MD, MSCE; Harris, Anthony D. MD, MPH

- Healthcare workers providing routine care in a 29-bed ICU at University of Maryland Medical Center
- Urban tertiary care academic hospital
- Cultures from hands prior and after entering a patient's room, gloves and gowns

*Infect Control Hosp Epidemiol*. July 2008 29(7): 583-8
Detection of Methicillin-Resistant *Staphylococcus aureus* and Vancomycin-Resistant Enterococci on the Gowns and Gloves of Healthcare Workers

Snyder, Graham M. MD; Thom, Kerri A. MD; Furuno, Jon P. PhD; Perencevich, Eli N. MD, MS; Roghmann, Mary-Claire MD, MS; Strauss, Sandra M. BS MT(ASCP); Netzer, Giora MD, MSCE; Harris, Anthony D. MD, MPH

**Table 1. Rates of Detection of Methicillin-Resistant *Staphylococcus aureus* (MRSA) and Vancomycin-Resistant Enterococci (VRE) on the Gowns and Gloves Worn by Healthcare Workers Caring for Patients with MRSA and VRE Carriage**

<table>
<thead>
<tr>
<th>Sample cultured</th>
<th>Patients with MRSA carriage</th>
<th>Patients with VRE carriage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Proportion of observations</td>
<td>Percentage of observations (95% CI)</td>
</tr>
<tr>
<td>Gloves</td>
<td>14/79</td>
<td>17.7 (9.3–26.1)</td>
</tr>
<tr>
<td>Gown</td>
<td>5/81</td>
<td>6.2 (1–11.4)</td>
</tr>
<tr>
<td>Gloves and/or gown</td>
<td>15/81</td>
<td>18.5 (10–27)</td>
</tr>
<tr>
<td>Hands after removing gloves and gown</td>
<td>2/78</td>
<td>2.6 (−0.9 to 6.1)</td>
</tr>
</tbody>
</table>

**Note.** For some interactions, gown or glove samples could not be obtained, so the total number of observations varies. CI, confidence interval.
Active Surveillance for Methicillin-Resistant Staphylococcus aureus (MRSA) Decreases the Incidence of MRSA Bacteremia

Pnina Shitrit, MD; Bat‐Sheva Gottesman, MD; Michal Katzir, MD; Avi Kilman, MSc; Yona Ben‐Nissan, BSc; Michal Chowers, MD

- 700 bed hospital
- Compared MRSA Bacteremia 13 months before and 15 months after intervention
- Intervention:
  - Surveillance of high risk patients
  - Contact precautions and isolation
  - Eradication

*Infect Control Hosp Epidemiol* 2006;27:1004–100
Active Surveillance for Methicillin-Resistant *Staphylococcus aureus* (MRSA) Decreases the Incidence of MRSA Bacteremia

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- Surveillance cultures at admission and once/month
  - Hospitalized in the previous month
  - Transferred from another hospital, ward, LTCF
  - Receiving long term HD
  - Known history of MRSA
  - All patients admitted to SICU or Geriatric ward

- Contact precautions and isolation
  - Single room when available
  - Gown and gloves for all patients
  - Mask for ventilated patients

- Eradication treatment
  - Mupirocin ointment to anterior nares TID
  - Chlorhexidine showers daily X 5 days

*Infect Control Hosp Epidemiol 2006;27:1004–100*
Episodes of MRSA Bacteremia Per Month

3.6 +/- 1.4/month  
P<0.001

1.4 +/- 0.8/month  
P<0.001

Figure. Number of episodes of methicillin-resistant Staphylococcus aureus (MRSA) bacteremia per month before (from January 2002 through February 2003) and after (from July 2003 through October 2004) initiation of active surveillance for MRSA.

*Infect Control Hosp Epidemiol* 2006;27:1004–100
Rapid Screening Tests for Methicillin-Resistant *Saphylococcus aureus* at Hospital Admission: Systematic Review and Meta-Analysis.

Tacconelli E, De Angelis G, de Waure C, Cataldo MA, La Torre G, Cauda R

- Meta-analysis of 10 studies comparing active screening of MRSA (rapid or culture) versus no screening

- Screening for MRSA significantly decreased MRSA bacteremia by 46%

Figure: Effect of rapid molecular tests for meticillin-resistant *Staphylococcus aureus* (MRSA) at hospital admission on the incidence of MRSA bloodstream infections per 1000 patient-days. Comparison is between units in which screening was done by molecular tests and units in which screening was not done at all. Risk ratios (RR) and their 95% CIs are shown (fixed effects). Dotted line indicates combined RR. Squares indicate point estimates and the size of the square indicates the weight of each study in the meta-analysis.

On the Home Front

• Patients over 18 years of age admitted to the Denver Health SICU and MICU were screened by nasal swab on admission and weekly for 15 months

• MRSA positive patients were considered infected and placed under contact precautions
  • Private room, gown, gloves
  • Warning attached to the patient record.

• MRSA rates were compared with the 15 months prior to screening intervention

Infect Control Hosp Epidemiol 2006;27:1009-17
Overall Rates of Total and Nosocomial MRSA Infections in DH MICU, SICU & Wards

Total P=0.01
Nosocomial P<0.01

Infect Control Hosp Epidemiol 2006;27:1009-17
Rates of Total MRSA Infections Versus Nosocomial MRSA Infections in DH SICU

Preintervention
- Total = 9.4 (mean)
- Nosocomial = 9.1 (mean)

Postintervention
- Total = 4.9 (mean)
- Nosocomial = 4.7 (mean)

Total P<0.005
Nosocomial P<0.002

Infect Control Hosp Epidemiol 2006;27:1009-17
Rates of Total MRSA Infections Versus Nosocomial MRSA Infections in DH MICU

Infect Control Hosp Epidemiol 2006;27:1009-17
### Table 2. Cost Analysis of the Methicillin-Resistant Staphylococcus aureus (MRSA) Screening Program at Denver Health Medical Center (Denver, CO)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cost of screening per month</strong></td>
<td></td>
</tr>
<tr>
<td>Swabs</td>
<td></td>
</tr>
<tr>
<td>Cost per swab</td>
<td>$0.25</td>
</tr>
<tr>
<td>Mean number of patients swabbed</td>
<td>330</td>
</tr>
<tr>
<td>Total</td>
<td>$82.50</td>
</tr>
<tr>
<td><strong>Microbiologic analysis</strong></td>
<td></td>
</tr>
<tr>
<td>Mean number MRSA-positive swabs</td>
<td>11</td>
</tr>
<tr>
<td>Cost per MRSA-positive swab</td>
<td>$5.50</td>
</tr>
<tr>
<td>Mean number MRSA-negative swabs</td>
<td>229</td>
</tr>
<tr>
<td>Cost for MRSA-negative swab</td>
<td>$1.24</td>
</tr>
<tr>
<td>Total</td>
<td>$337.36</td>
</tr>
<tr>
<td><strong>Total screening cost</strong></td>
<td>$419.86</td>
</tr>
<tr>
<td><strong>Cost of isolation per month</strong></td>
<td></td>
</tr>
<tr>
<td>Cost of 1 pair of gloves</td>
<td>$0.08</td>
</tr>
<tr>
<td>Cost of 1 gown</td>
<td>$0.10</td>
</tr>
<tr>
<td>Cost of 60 s of nursing time</td>
<td>$0.47</td>
</tr>
<tr>
<td>Estimated no. of patient contacts per day</td>
<td>100</td>
</tr>
<tr>
<td>Estimated cost per patient per day</td>
<td>$65.00</td>
</tr>
<tr>
<td>Mean total excess isolation-days</td>
<td>47</td>
</tr>
<tr>
<td>Excess isolation cost</td>
<td>$3,055.00</td>
</tr>
<tr>
<td><strong>Cost avoidance per month</strong></td>
<td></td>
</tr>
<tr>
<td>Averted no. of ICU infections</td>
<td>2.5</td>
</tr>
<tr>
<td>Excess cost of 1 MRSA infection</td>
<td>$9,275.00</td>
</tr>
<tr>
<td>Cost savings of averted cases</td>
<td>$23,188.00</td>
</tr>
<tr>
<td>Less excess isolation cost</td>
<td>$3,055.00</td>
</tr>
<tr>
<td>Less total screening cost</td>
<td>$419.86</td>
</tr>
<tr>
<td>Overall cost avoidance for ICUs</td>
<td>$19,714.00</td>
</tr>
</tbody>
</table>

*Infect Control Hosp Epidem 2006;27:1009-17*
Conclusion

- MRSA is a serious infection
- Effective abroad. Effective at home
- Decreased MRSA infections and bacteremia
- Decreased cost
The Real Question?

- Should we be screening healthcare workers?
- Should we be eradicating MRSA once found on screening?


• **Hospital infection control strategies for vancomycin-resistant Enterococcus, methicillin-resistant *Staphylococcus aureus* and Clostridium difficile** CMAJ. 2009 Mar 17;180(6):627-31


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• Klevens RM et al. Clinical Infectious Diseases 2006;42:389-91


• Gorwitz RJ et al. *Journal of Infectious Diseases*. 2008;197;1226-34
Questions?